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PATENT SPECIFICATION

NO DRAWINGS

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COMPLETE SPECIFICATION

Improvements in or relating to Extracts of Marrubium

I, VICTOR LAFON, of 76 avenue de la République, Paris, France, of French nationality, do hereby declare the invention, for which I pray that a patent may be granted to me, and the method by which it is to be performed, to be particularly described in and by the following statement:—

The present invention relates to a process for forming a spray-dried product from an extract of Marrubium, the spray-dried product formed by the process and pharmaceutical compositions containing the spray-dried product.

In the preparation of the spray-dried product, the raw material used is Marrubium Vulgare, from the family of Labiatae.

Marrubium Vulgare is also commonly known by the names Hoarhound of White Horehound.

According to the present invention, a process of producing a Marrubium spray-dried product comprises subjecting parts of Marrubium Vulgare to extraction with an aqueous solvent at a temperature not greater than 100°C. and spray-drying the extract at a temperature not greater than 60°C.

The parts of the plant most suitable for use in the process according to the invention are the leaves and/or the flowers. The spray-drying of the extract, preferably obtained with water, is advantageously carried out at a temperature ranging from 40°C to 60°C.

A method of preparing the product of the invention is given below by way of example.

1 kg. of powdered leaves and flowers of Marrubium Vulgare was added to 6 litres of water at 100°C. The solution containing the powder was maintained at 100°C for 6 hours and was then filtered. The infused solution was mixed in a mixing machine and afterwards projected as a spray from capillary jets under a pressure of about 250 Kg./cm² into a vessel traversed by a strong blast of air. This operation was carried out at a temperature in the region of 55°C.

A fine powder deposited on the bottom of the vessel.

The product has entirely new properties compared with known extracts of Marrubium which can be prepared at the moment by known processes.

It has practically no toxic effect; it has an anti-spasmodic action; it is very hypocholeretic; it diminishes the hypertensive effect of adrenalin and has an antiserotonin action.

Its hypocholeretic character is particularly interesting and is the main difference between it and the known extracts of Marrubium which have a very marked hypercholeretic action.

Results of test carried out with the product according to the invention are given below:

The toxicity was determined by intraperitoneal administration to mice.

Doses of 1.2 g/kg. did not kill any of the mice. Doses of 4 g/kg were fatal to the mice.

The product according to the invention is anti-spasmodic. Evidence of this action has been obtained by studying its musculotropic effect *in vitro* according to Magnus' method, (Arch. Ges. Physiol., 1904, c11, pp. 123 and 349) on the duodena of six rats suffering from spasms induced by barium chloride. The effective dose is 1 mg./cm³ of solution, made using Tyrode liquid as the solvent.

For determining its neurotropic effect, the action of the product on six isolated rats duodena subjected to spasms induced by acetylcholine was studied.

The most effective dose was 0.93 mg./cm³ of solution in Tyrode liquid.

This action determined *in vitro* has been confirmed *in vivo* on rabbits and dogs, for

which doses of 50 mg./kg. administered by intravenous injection produced a very marked action, involving suppression of the customary spasm.

The gastro-intestinal action has been studied. The gastro-intestinal transit has particularly been studied by the coloured meal method on mice.

Doses of 50 and 100 mg./kg. administered by intra-peritoneal injection have caused a marked retardation of transit.

On dogs having a temporary choledoch fistula, doses of 10 to 50 mg./kg. administered by intraperitoneal injection produced a very marked hypocholeretic effect.

In studying the cardio-vascular action of the product, doses of 10 to 50 mg./kg. were administered to dogs and cats by intravenous injection and produced a marked hypotension of 30 to 70%, without causing cardiac action.

The antiserotonin action has been studied on isolated guinea-pig ileum, the product in a dose of 466 mg/cm³ of solution in Tyrode liquid reduced the contraction caused by serotonin by 50%. On the uterus of a rat, the most efficacious dose has been determined as 3.33 mg/cm³ Ringer's solution.

The action has been confirmed on serotonin-induced oedema in rat paws and by the Woolley test (Proc. Soc. Exp. Biol. Med., 1958, Vol. 98, p. 367) and the Corne test (Brit. J. Pharmacol., 1963, Vol. 20, p. 106).

Finally a clinical study has been made on humans by means of tablets containing 0.50 g. of the spray-dried product. When absorbed over a period of 3 to 6 days they suppress migraine caused by digestive troubles and hepatic colic. They suppress and prevent pain and nausea in a test with sodium dehydrocholate and morphine.

Pharmaceutical compositions having useful applications are prepared from the Marrubium spray-dried product and a pharmaceutical carrier. Tablets and cachets containing from 0.25 g. to 0.50 g. of the Marrubium spray-dried product are useful for its oral administration.

One form of tablet incorporating the spray-dried product of the invention has the following composition:

Marrubium spray-dried product	0.25 g.
Calcium carbonate	0.10 g.
Starch	0.05 g.
Magnesium stearate	0.01 g.
Shellac	0.003 g.
Gum arabic	0.004 g.
Talc	0.110 g.
Sugar q.s.	0.70 g.

for a sugar-coated tablet.

In addition to the above uses of the product, these tablets, as well as cachets, are useful for preventing post-prandial flushing of the face and as anti-diarrhoeaics.

WHAT I CLAIM IS:—

1. A process of producing a Marrubium spray-dried product, which comprises subjecting parts of Marrubium Vulgare to extraction with an aqueous solvent at a temperature not greater than 100°C. and spray-drying the extract at a temperature not greater than 60°C.

2. A process as claimed in claim 1, in which the parts subjected to extraction are leaves and/or flowers.

3. A process as claimed in claim 1 or 2, in which the solvent is water.

4. A process as claimed in any preceding claim, in which spray-drying is effected at a temperature ranging from 40°C. to 60°C.

5. A process of producing a Marrubium spray-dried product as claimed in claim 1, substantially as hereinbefore described.

6. A Marrubium spray-dried product, when produced by a process as claimed in any preceding claim.

7. A pharmaceutical composition, which comprises a Marrubium spray-dried product as claimed in claim 6 and a pharmaceutical carrier.

8. A tablet or cachet formed from a pharmaceutical composition as claimed in claim 7, which comprises 0.25 g. to 0.50 g. of the Marrubium spray-dried product.

9. A sugar-coated tablet of the composition:

Marrubium spray-dried product	0.25 g.
Calcium carbonate	0.10 g.
Starch	0.05 g.
Magnesium stearate	0.01 g.
Shellac	0.003 g.
Gum arabic	0.004 g.
Talc	0.110 g.
Sugar q.s.	0.70 g.

POLLAK, MERCER & TENCH,
Chartered Patent Agents,
Audrey House,
Ely Place,
London, E.C.1.
Agents for the Applicant.

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